DETAILED OFFICE ACTION

Rejection Under 35 USC 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-11, 13, 31-36, and 40 are rejected under 35 USC 112, paragraph 2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 2, 5 and 40, the "or" between the definitions of R3 and R4 should be changed to read -- and --, or it should be deleted.

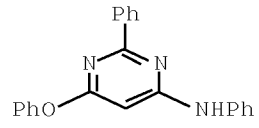
In claim 31, the meaning of "active compound" is not understood. The purpose for which it is active is undefined. In claims 32-34, ultimately dependent on claim 31, because "active compound" is undefined in claim 31, the purpose of the additional compounds is not understood.

Rejection Under 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

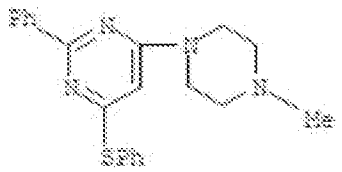
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 13, and 31 are rejected under 35 USC 102(b) over Sugiura, et al., JP 11158073, published 19990615, describing:
RN228575-20-0, 4-Pyrimidinamine, 6-phenoxy-N,2-diphenyl-,

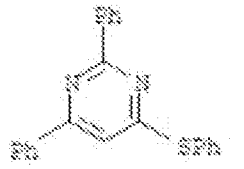


, as Adenosine A3 antagonists.

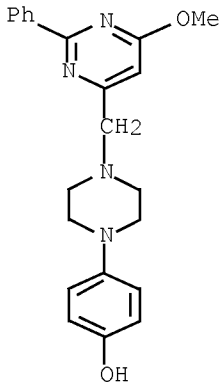
Claims 1-4, 6, 8-11, 13, 31 and 40 are rejected under 35 USC 102(b) over Santilli, et al., US 3498984, issued 03-03-1970, describing the compounds of formula in col. 1 and the corresponding species of the examples, see e.g., Example VIII


, possessing anti-viral, anticonvulsant, antibacterial, hypotensive and anti-inflammatory activity.

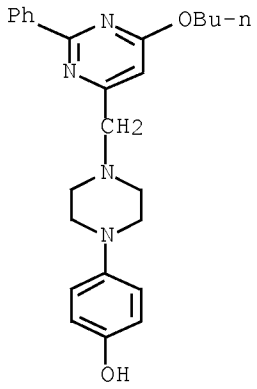
Claims 1, 11, 13, and 31 are rejected under 35 USC 102(b) over Herrera, Tetrahedron, 59 (2003), 7331-7336, describing formula 4


.

Claims 1, 11, 13, and 31 are rejected under 35 USC 102(b) over Kampe, et al., US 4859670, issued 19890822, describing:
RN111921-21-2, Phenol, 4-[4-[(6-methoxy-2-phenyl-4-pyrimidinyl)methyl]-1-piperazinyl]-
,

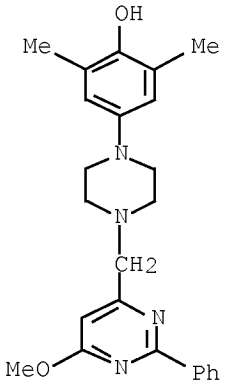


,
RN111921-25-6, Phenol, 4-[4-[(6-butoxy-2-phenyl-4-pyrimidinyl)methyl]-1-piperazinyl]-,



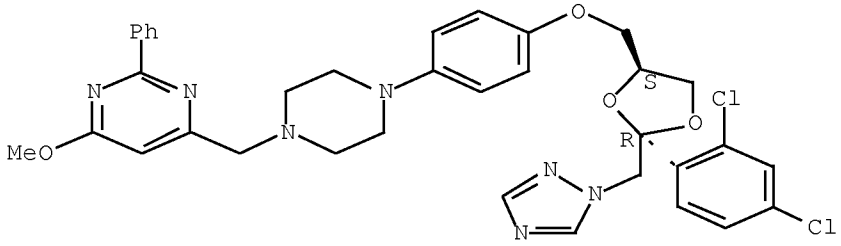
,

RN111921-26-7, Phenol, 4-[4-[(6-methoxy-2-phenyl-4-pyrimidinyl)methyl]-1-piperazinyl]-2,6-dimethyl-,



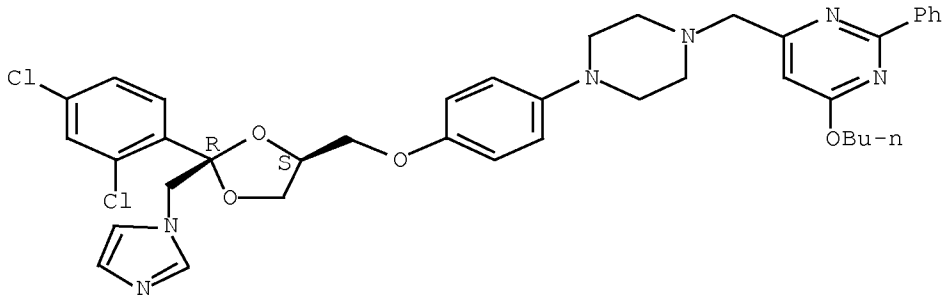
,

RN111920-67-3, Pyrimidine, 4-[[4-[4-[[(2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]methyl]-6-methoxy-2-phenyl-,

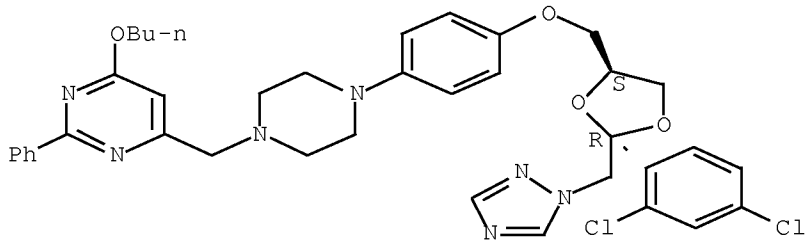


,

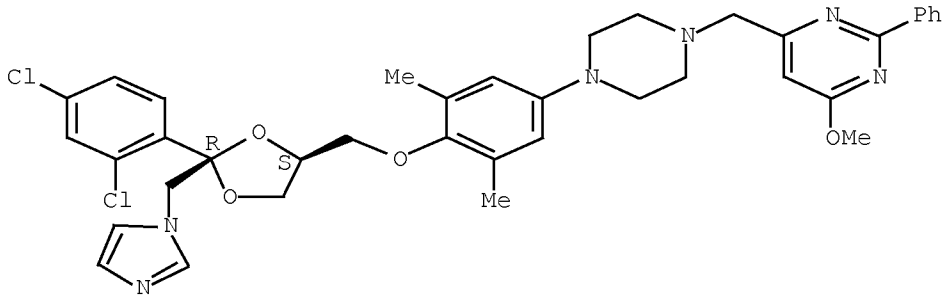
RN111920-68-4, Pyrimidine, 4-butoxy-6-[[4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]methyl]-2-phenyl-, cis-,



,
RN111920-69-5, Pyrimidine, 4-butoxy-6-[[4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]methyl]-2-phenyl-,

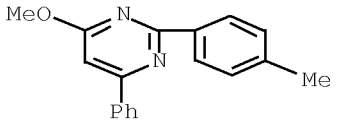


,
RN111920-75-3, Pyrimidine, 4-[[4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]-3,5-dimethylphenyl]-1-piperazinyl]methyl]-6-methoxy-2-phenyl-,



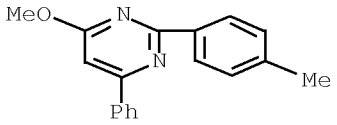
, as medical fungicides.

Claims 1, 11, 13, 31 and 40 are rejected under 35 USC 102(b) over Seiler, et al., EP 136976 A3, published 19850515, describing:
RN77232-23-6, Pyrimidine, 4-methoxy-2-(4-methylphenyl)-6-phenyl-,



, to protect crop plants against phytotoxic damage caused by herbicides.

Claims 1, 11, 13, 31 and 40 are rejected under 35 USC 102(b) over Burdeska, et al., EP 55693 A1, published 19820707, describing:
RN77232-23-6, Pyrimidine, 4-methoxy-2-(4-methylphenyl)-6-phenyl-,



, as protecting agents for crop plants against phytotoxic damage caused by herbicides.

Rejections Under 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering claim patentability under 35 USC 103(a), the examiner presumes that the subject matter of the various claims was commonly owned when any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly

owned when a later invention was made so the examiner can applicability of 35

USC 103(c) and potential 35 USC 102(e), (f) or (g) prior art under 35 USC 103(a).

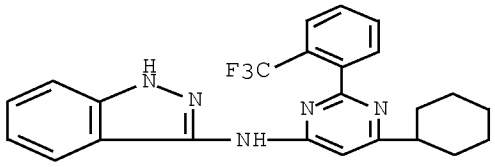
Claims 1-4, 6, 11, 13, 31 and 40 are rejected under 35 USC 103(a) over Santilli, et al., US 3,498,984, issued 03-03-1970. The presently claimed compounds are alkyl homologs and/or position isomers of the Santilli compounds and obvious thereover as for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

It would have been obvious to one of ordinary skill in the art at the time the present invention was made to modify the compounds of SantilII to prepare compounds homologous and/or isomeric therewith. One of ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous and/or isomeric compounds are expected to possess similar properties to the SantilII compounds. It has been held that compounds that are structurally homologous and/or isomeric to prior art compounds are *prima facie* obvious, absent a showing of unexpected results.

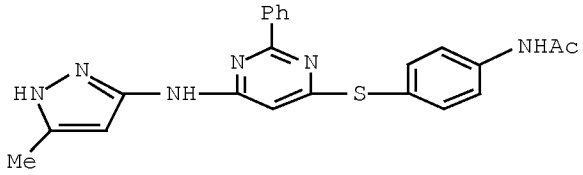
> An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.

In re Payne, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 16 USPQ2d 1897 (Fed.Cir. 1991) (discussed in MPEP § 2144) for an extensive case law review of obviousness based on close structural chemical compound similarity. See MPEP § 2144.08, ¶ II.A.4(c). Compounds which are homologs (compounds differing regularly by the successive addition or subtraction of the same chemical group, e.g., by methyl or lower alkyl groups), and/or isomeric (compounds differing by having a particular substituent in a neighboring position) as here, are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 195 USPQ 426 (CCPA 1977). Absent the presentation of unobvious properties for the compounds of the present claims over those of Santilli, these claims cannot be deemed patentable.

Claims 1, 11, 13, 31 and 40 are rejected under 35 USC 103(a) over Knegtel, et al., US 6613776, issued 20030902, describing:
RN404827-52-7, 1H-Indazol-3-amine, N-[6-cyclohexyl-2-[2-(trifluoromethyl)phenyl]-4-pyrimidinyl]-,

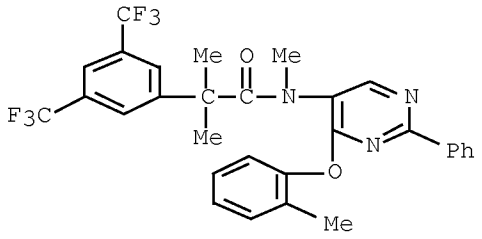


, and
RN404829-30-7, Acetamide, N-[4-[[6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-phenyl-4-pyrimidinyl]thio]phenyl]-,

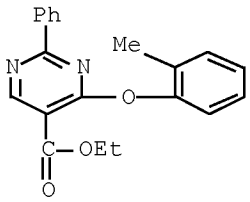


, to treat cancer, diabetes and Alzheimer's disease. The presently claimed compounds are alkyl homologs and/or position isomers of the Knegtel compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

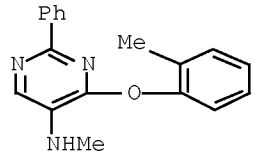
Claims 1-6, 8-11, 13, 31 and 40 are rejected under 35 USC 103(a) over Stadler, WO 2002042280, published 20020530, describing:
RN432521-49-8, Benzeneacetamide, N,α,α-trimethyl-N-[4-(2-methylphenoxy)-2-phenyl-5-pyrimidinyl]-3,5-bis(trifluoromethyl)-,



,
RN432521-69-2, 5-Pyrimidinecarboxylic acid, 4-(2-methylphenoxy)-2-phenyl-, ethyl ester,

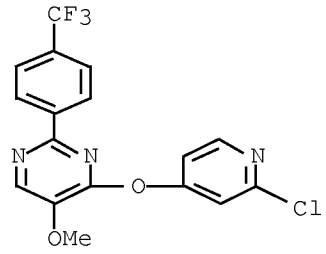


,
RN432521-73-8, 5-Pyrimidinamine, N-methyl-4-(2-methylphenoxy)-2-phenyl-,

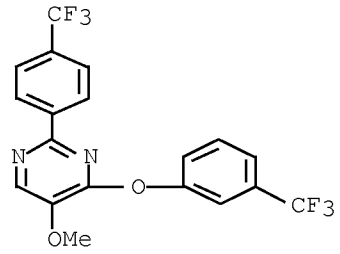


, as NK1 antagonists. The presently claimed compounds are alkyl homologs and/or position isomers of the Stadler compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

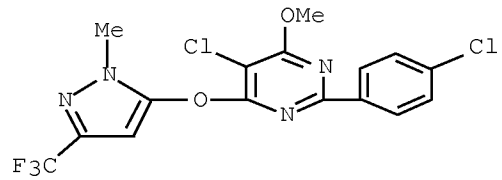
Claims 1-6, 8-11, 13, 31 and 40 are rejected under 35 USC 103(a) over Kleemann, et al. (I), US 5849758, issued 19981215, describing:
RN180607-27-6, Pyrimidine, 2-(3-chlorophenyl)-5-methyl-4-[[1-methyl-3-(trifluoromethyl)- 1H-pyrazol-5-yl]oxy]-,
RN180607-89-0, Pyrimidine, 4-[(2-chloro-4-pyridinyl)oxy]-5-methoxy-2-[4-(trifluoromethyl)phenyl]-,



,
RN180607-90-3, Pyrimidine, 5-methoxy-4-[3-(trifluoromethyl)phenoxy]-2-[4-(trifluoromethyl)phenyl]-,



,
RN180607-92-5, Pyrimidine, 5-chloro-2-(4-chlorophenyl)-4-methoxy-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,



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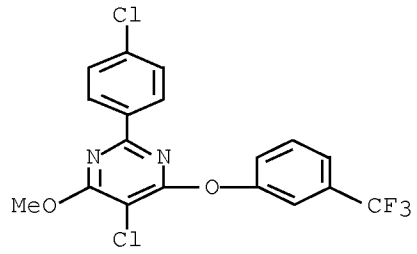
(trifluoromethyl)phenoxy]-,



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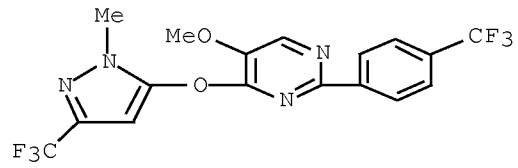
RN180607-96-9, Pyrimidine, 5-methoxy-4-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



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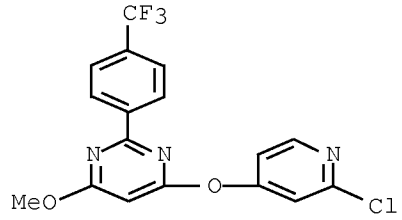
RN180608-05-3, Pyrimidine, 4-[(2-chloro-4-pyridinyl)oxy]-6-methoxy-2-[4-(trifluoromethyl)phenyl]-,



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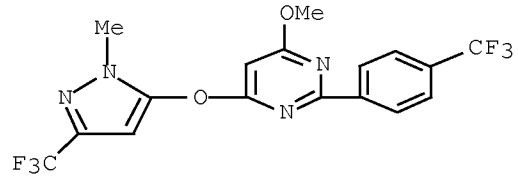

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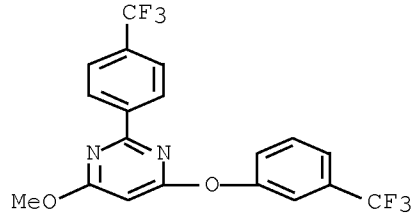
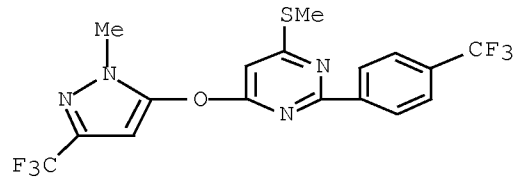


,

RN180608-09-7, Pyrimidine, 4-(methylthio)-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



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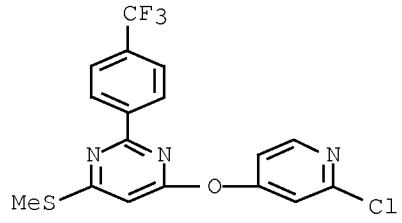

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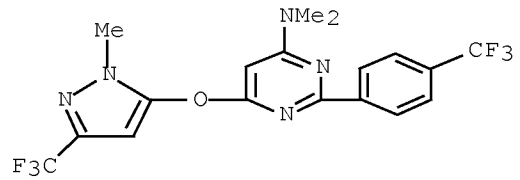
RN180608-11-1, 4-Pyrimidinamine, N,N-dimethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



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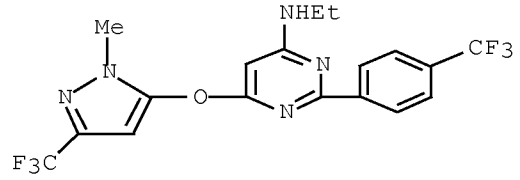
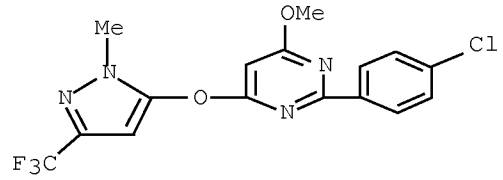
RN180608-12-2, 4-Pyrimidinamine, N-ethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



,

RN180608-13-3, Pyrimidine, 2-(4-chlorophenyl)-4-methoxy-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,



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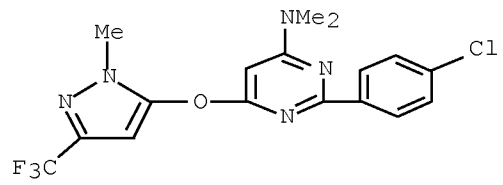
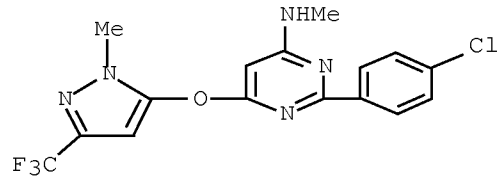
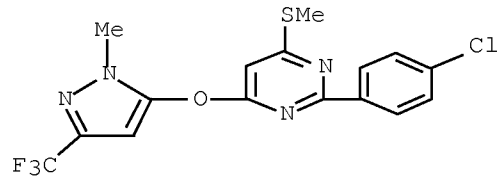
RN180608-15-5, 4-Pyrimidinamine, 2-(4-chlorophenyl)-N,N-dimethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,



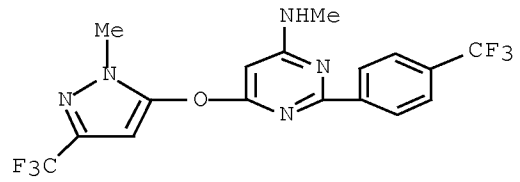
,
RN180608-17-7, 4-Pyrimidinamine, 2-(4-chlorophenyl)-N-methyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,



,
RN202994-71-6, Pyrimidine, 2-(4-chlorophenyl)-4-(methylthio)-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,

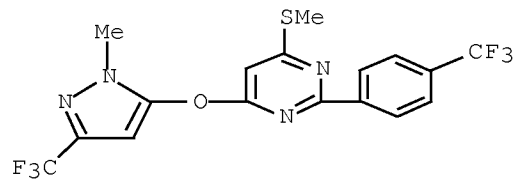


,
RN202994-96-5, 4-Pyrimidinamine, N-methyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,

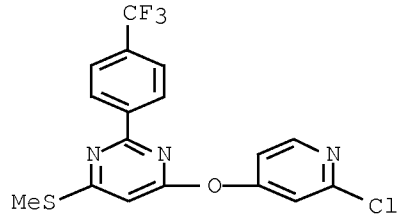


, as herbicides. The presently claimed compounds are alkyl homologs and/or position isomers of the Kleemann (I) compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

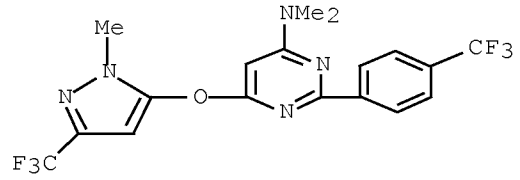
Claims 1-6, 8-11, 13, 31 and 40 are rejected under 35 USC 103(a) over Kleemann, et al. (II), US 5824624, issued 19981020, describing:
RN180608-09-7, Pyrimidine, 4-(methylthio)-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



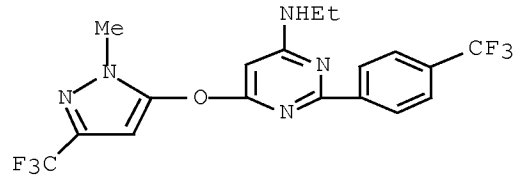
RN180608-10-0, Pyrimidine, 4-[(2-chloro-4-pyridinyl)oxy]-6-(methylthio)-2-[4-(trifluoromethyl)phenyl]-,



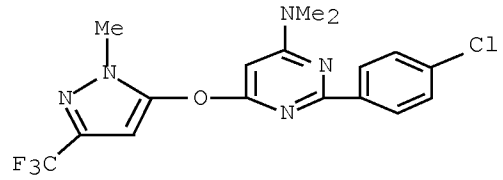
RN180608-11-1, 4-Pyrimidinamine, N,N-dimethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



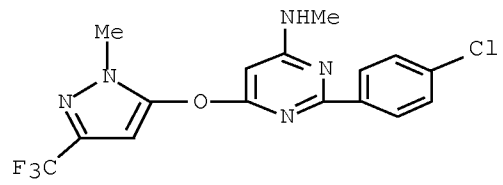
RN180608-12-2, 4-Pyrimidinamine, N-ethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



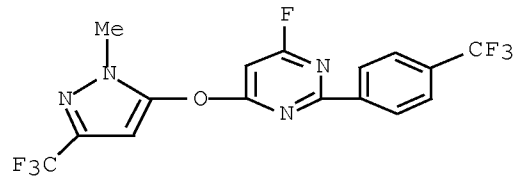
RN180608-15-5, 4-Pyrimidinamine, 2-(4-chlorophenyl)-N,N-dimethyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,



RN180608-17-7, 4-Pyrimidinamine, 2-(4-chlorophenyl)-N-methyl-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-,

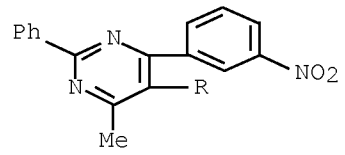


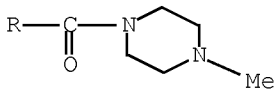
,
RN180608-35-9, Pyrimidine, 4-fluoro-6-[[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]oxy]-2-[4-(trifluoromethyl)phenyl]-,



, as herbicides. The presently claimed compounds are alkyl homologs and/or position isomers of the Kleemann (II) compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

Claims 1-6, 8-11, 13, 31 and 40 are rejected under 35 USC 103(a) over Sugiyama, et al., Chem. & Pharm. Bull. (1994), 42(6), 1279-85, describing:
RN103294-21-9, Methanone, [4-methyl-6-(3-nitrophenyl)-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)-,





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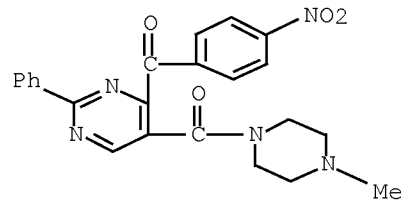
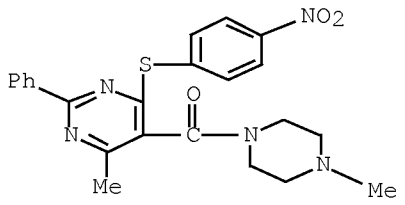
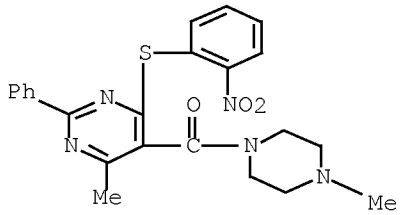
RN116904-25-7, Piperazine, 1-methyl-4-[[4-(4-nitrobenzoyl)-2-phenyl-5-pyrimidinyl]carbonyl]-,



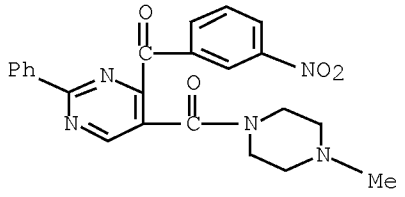
,
RN116904-26-8, Methanone, [4-methyl-6-[(4-nitrophenyl)thio]-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)-,



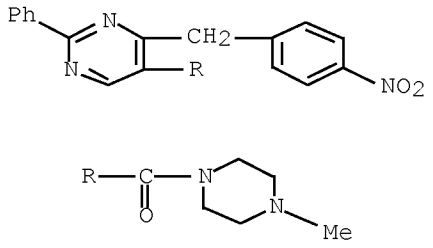
RN116904-27-9, Methanone, [4-methyl-6-[(2-nitrophenyl)thio]-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)-,



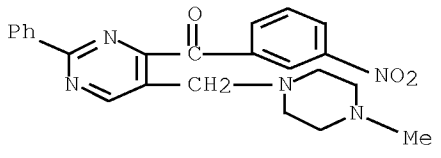
RN116904-30-4, Piperazine, 1-methyl-4-[[4-(3-nitrobenzoyl)-2-phenyl-5-pyrimidinyl]carbonyl]-,



RN116904-35-9, Methanone, (4-methyl-1-piperazinyl)[4-[(4-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-,

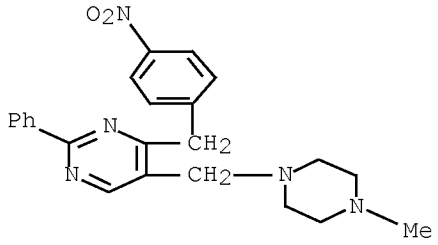


RN116904-53-1, Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl](3-nitrophenyl)-,



RN116904-65-5, Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(4-

nitrophenyl)methyl]-2-phenyl-,



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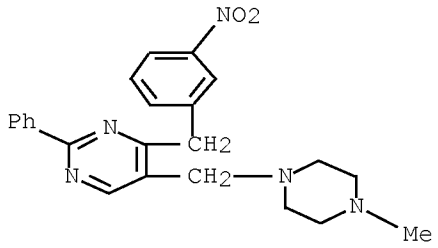
RN116904-66-6, Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(3-nitrophenyl)methyl]-2-phenyl-,



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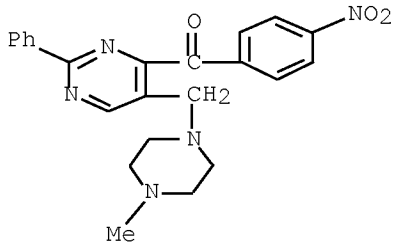
RN116924-80-2, Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl](4-nitrophenyl)-,



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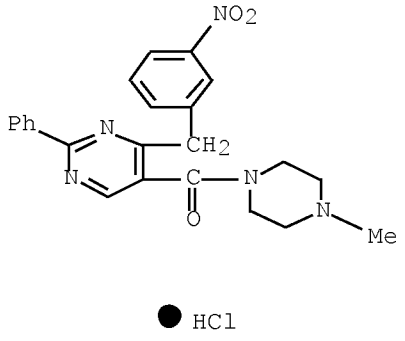
RN159970-99-7, Methanone, (4-methyl-1-piperazinyl)[4-[(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-, hydrochloride,



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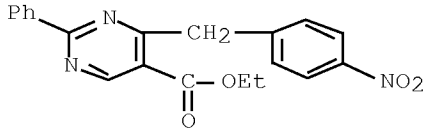
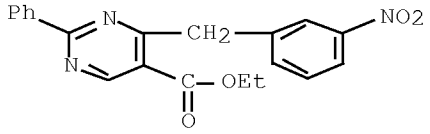
RN116904-36-0, 5-Pyrimidinecarboxylic acid, 4-[(4-nitrophenyl)methyl]-2-phenyl-, ethyl ester,



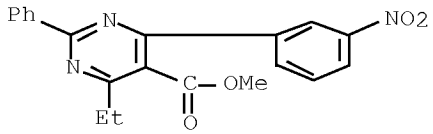
,

RN159971-02-5, 5-Pyrimidinecarboxylic acid, 4-[(3-nitrophenyl)methyl]-2-phenyl-, ethyl ester,



, with antianoxic activity. The presently claimed compounds are alkyl homologs and/or position isomers of the Sugiyama compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

Claims 1-6, 8-11, 13, 31 and 40 are rejected under 35 USC 103(a) over Takatani, et al., JP 63107966, published 19880512, describing:
RN103311-82-6, 5-Pyrimidinecarboxylic acid, 4-ethyl-6-(3-nitrophenyl)-2-phenyl-, methyl ester,



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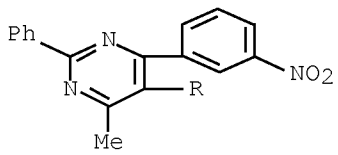
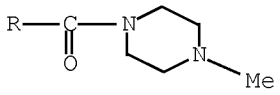
RN103294-21-9, Methanone, [4-methyl-6-(3-nitrophenyl)-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)-,





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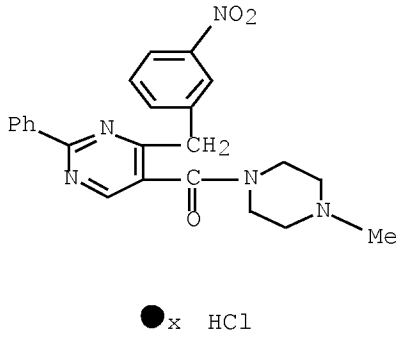
RN116904-34-8, Methanone, (4-methyl-1-piperazinyl)[4-[(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-, hydrochloride,



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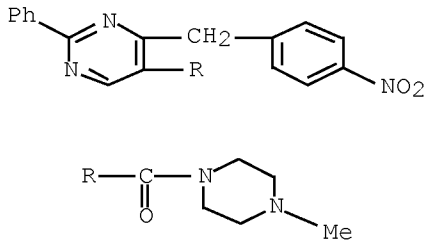
RN116904-35-9, Methanone, (4-methyl-1-piperazinyl)[4-[(4-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-,



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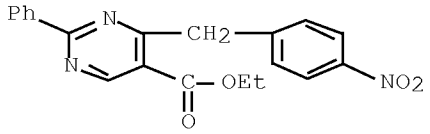
RN116904-36-0, 5-Pyrimidinecarboxylic acid, 4-[(4-nitrophenyl)methyl]-2-phenyl-, ethyl ester,



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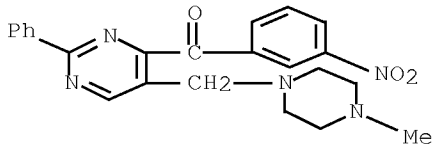
RN116904-53-1, Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl](3-nitrophenyl)-,



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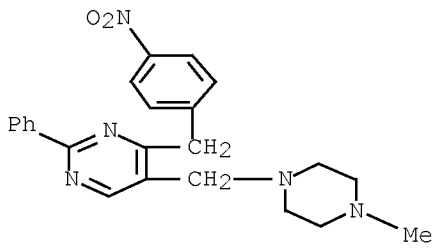
RN116904-65-5, Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(4-nitrophenyl)methyl]-2-phenyl-,



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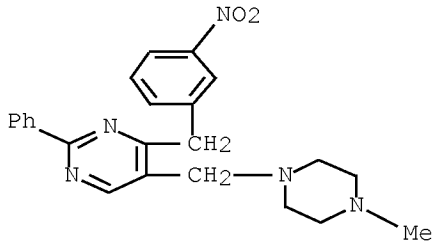
RN116904-66-6, Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(3-nitrophenyl)methyl]-2-phenyl-,



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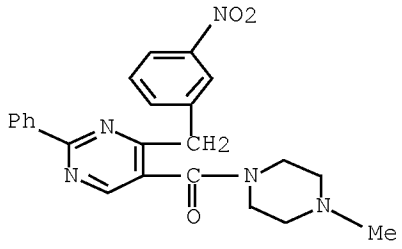
RN116904-78-0, Methanone, (4-methyl-1-piperazinyl)[4-[(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-,



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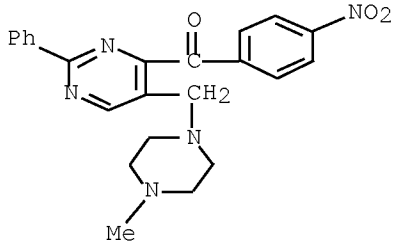
RN116924-80-2, Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl](4-nitrophenyl)-,



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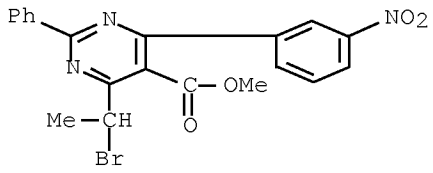
RN116904-73-5, 5-Pyrimidinecarboxylic acid, 4-(1-bromoethyl)-6-(3-nitrophenyl)-2-phenyl-, methyl ester,



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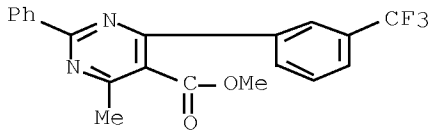
RN116904-77-9, 5-Pyrimidinecarboxylic acid, 4-methyl-2-phenyl-6-[3-(trifluoromethyl)phenyl]-, methyl ester,



, as drugs for treating disease and disorders of cerebral blood vessels. The presently claimed compounds are alkyl homologs and/or position isomers of the Takatani compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

Claims 1, 11, 13, 31 and 40 are rejected under 35 USC 103(a) over Kampe, et al., US 4859670, issued 19890822, as medical fungicides. The presently claimed compounds are alkyl homologs and/or position isomers of the Kampe compounds and obvious thereover for the same utility. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

Claims 1, 11, 13, 31 and 40 are rejected under 35 USC 103(a) over Burdeska, et al. (I), US 4493726, issued 19850115. The presently claimed compounds are alkyl homologs and/or position isomers of the Burdeska (I) compounds and obvious thereover as antidotes for protecting cultivated plants against phytotoxic damage caused by herbicides. See the discussion above of the obviousness of homologs and/or isomers over prior art compounds to the same utility.

Allowed Claim

Claim 14 is allowed. Following is an examiner's statement of reasons for indicating allowance.

Each of the references cited above against the remaining claims describe certain substituted pyrimidines, but the compounds of claim 14 each have certain substituents

which are neither shown nor suggested by these references. In addition, claim 14 recites compounds which are neither anticipated nor rendered obvious by any of the prior art of record, whether taken individually or in any combination.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle whose telephone number is (571)272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. If you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia M. Jaisle/
Examiner, Art Unit 1624

/JAMES O. WILSON/
Supervisory Patent Examiner, Art Unit 1624